

WEST Search History

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DB=USPT,PGPB,EPAB,DWPI; PLUR=YES; OP=ADJ

L1	short PCR	129	L1
L2	detect same (mutation or deletion or mutant)	11039	L2
L3	l1 and l2L2	0	L3
L4	l1 and l2	42	L4
L5	L4 and (mitochondrial DNA or mt-DNA)	5	L5
L6	l1 and (mitochondrial DNA or mt-DNA)	7	L6
L7	l2 and (mitochondrial DNA or mt-DNA)	305	L7
L8	L7 and (cleav\$ agent or cleav\$ reagent or cleav\$)	225	L8
L9	l8 and amplicon	50	L9
L10	L9 and (PCR or polymerase chain reaction)	50	L10
L11	L10 and ((mutant near primer) or mutant PCR primer or (primer near mismatch))	3	L11
L12	sutherland-J\$.in.	277	L12
L13	L12 and PCR	23	L13

END OF SEARCH HISTORY

Non-symmetric polymerase chain

reaction amplification, useful for amplifying DNA by thermally cycling a **PCR** reaction mixture containing a DNA amplification target sequence, a pair of **PCR** primers, dNTP's and thermostable polymerase;

DNA primer and DNA probe for use in disease diagnosis

AUTHOR: WANGH L J; PIERCE K; HARTSHORN C; RICE J; SANCHEZ J A
PATENT ASSIGNEE: UNIV BRANDEIS
PATENT INFO: WO 2003054233 3 Jul 2003
APPLICATION INFO: WO 2002-US40752 19 Dec 2002
PRIORITY INFO: US 2002-320893 17 Dec 2002; US 2001-341886 19 Dec 2001
DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: WPI: 2003-569258 [53]
AN 2003-20602 BIOTECHDS
AB DERWENT ABSTRACT:

NOVELTY - Non-symmetric polymerase chain

reaction (PCR) amplification comprising thermally cycling a **PCR** reaction mixture containing a DNA amplification target sequence, a pair of **PCR** primers, dNTP's and thermostable polymerase repeatedly through **PCR** steps of strand melting, primer annealing, and primer extension, is new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following: (1) a homogenous detection assay for at least one DNA amplification target sequence employing the non-symmetric **PCR** amplification; (2) amplification of nucleic acid target sequence present in a sample containing up to 10000 copies of the target sequence; (3) an oligonucleotide set comprising a pair of primers for amplifying a selected DNA sequence by a non-symmetric **PCR**; and (4) a kit of reagents for performing a homogeneous **PCR** assay for at least one pre-selected DNA target sequence comprising at least one pair of **PCR** primers including a first and second primer, four deoxyribonucleotide triphosphates, a thermostable DNA polymerase, and a labeled hybridization probe that emits a detectable signal upon hybridization.

BIOTECHNOLOGY - Preferred Method: In the non-symmetric **PCR** method, at the onset of amplification, the reaction mixture contains up to 1000000 copies of the amplification target sequence; the **PCR** primer pair comprises a limiting primer at a concentration of up to 200 nM and an excess primer at a concentration of at least five times higher than the limiting primer; the initial concentration-adjusted melting temperature of the limiting primer is equal to or greater than the initial concentration-adjusted melting temperature of the excess primer; if the limiting primer is not fully complementary to the concentration-adjusted melting temperature of that portion of the limiting primer that hybridizes to the target sequence is not more than 5 degrees Centigrade below the concentration-adjusted melting temperature of the excess primer; the melting temperature of the **amplicon** produced by extension of the excess primer exceeds the initial concentration-adjusted melting temperature of the excess primer by not more than 18 degrees Centigrade; and thermal cycling is repeated a number of times sufficient to include multiple cycles of linear amplification using the excess primer following exhaustion of the limiting primer. The reaction mixture includes a pair of **PCR** primers for each target, and where the initial concentration-adjusted melting points of all limiting primers are equal to or greater than the initial concentration-adjusted melting points of all excess primers. The method further comprises reverse transcribing an RNA molecule to generate the DNA target sequence. The reaction mixture contains up to 50000 copies of the nucleic acid target. The initial concentration-adjusted melting temperature of the limiting primer is at least 3 degrees Centigrade higher than that of the excess primer. The melting temperature of the **amplicon** is 7-15 degrees Centigrade higher than the initial concentration-adjusted melting point of the excess primer. The reaction

mixture contains up to 1000 copies of the DNA target. The duration of primer annealing step is not longer than 30 seconds. The method further includes at least one terminal thermal cycle in which the single-stranded extension product of the excess primer is converted to double-stranded product, where the PCR reaction mixture additionally includes a low-temperature primer capable of priming the extension product of the excess primer. The reaction mixture additionally contains a complementary oligonucleotide that hybridizes to the 3'-end of the excess primer and has an initial concentration-adjusted melting temperature at least 3 degrees Centigrade lower than the initial, concentration-adjusted melting temperature of the excess primer. The complementary oligonucleotide is present at the outset in a concentration greater than the concentration of the excess primer. The method can additionally comprise, during at least some cycles of linear amplification, following the step of primer extension product of the excess primer from the reaction mixture by hybridizing the product to capture probes. The capture probes are in a thermally isolated product removal zone and the step of removing comprises passing the reaction mixture through the zone. Where product removal zone is physically isolatable from the at least one reaction zone, the method further includes periodically isolating the product removal zone and harvesting product hybridized to the capture probes while the reaction mixture is in the at least one reaction zone. The initial concentration-adjusted melting temperature of the limiting primer is at least 3 degrees Centigrade higher than that of the excess primer. The melting temperature of the amplicon exceeds the initial concentration-adjusted melting temperature of the excess primer by not more than 18 degrees Centigrade. the excess primer is present at a concentration of 500-2000 nM and at least ten times higher than the limiting primer. The detection assay is end-point detection. The step of detection is **real time** detection that is performed during the annealing step of at least some cycles of linear amplification, or following the extension step of at least some cycles of linear amplification and prior to strand melting of the following cycles. The duration of the primer annealing is not longer than 30 seconds. The at least one hybridization probe is a dual labeled fluorescent probe that hybridizes to the extension product of the limiting primer and that is hydrolyzed by the polymerase during extension of the excess primer, thus generating a detectable signal. At least one hybridization probe emits a detectable signal upon hybridization to the extension product of the excess primer, and comprises a first probe for one allelic **variant** and a second probe for another allelic **variant**. The assay further comprises reverse transcribing of the RNA molecule to generate the DNA target sequence. The initial concentration-adjusted melting temperature of the low-temperature hybridization probe is at least 10 degrees Centigrade below than that of the limiting primer. Each probe is present in the reaction mixture at a concentration of at least 1 microM. The PCR amplification includes an added detection step following primer extension during at least some cycles of linear amplification. The detection step is of sufficiently low temperature and sufficient duration for the low temperature hybridization probes to hybridize and signal, and where the PCR step of primer annealing is not of sufficiently low temperature and sufficient duration of the probes to hybridize and signal. The detection step is preformed only beginning a few cycles prior to the threshold cycle of the reaction. The low-temperature detecting step is not more than 30 seconds duration. The detection is an end-point detection following completion of the amplification reaction. The method for amplification of nucleic acid target sequence present in a sample containing up to 10000 copies of the target sequence comprises contacting the nucleic acid target sequence with a first oligonucleotide primer and a second nucleotide primer, where the T_m of the first primer is at least 5 degrees Centigrade greater than the T_m of the second primer and where the concentration of the second primer is up to 1000 nM and at least about 10 times greater than the concentration of the first primer; and amplifying the target sequence by

PCR utilizing the first and second oligonucleotide primers, where the reaction has an exponential phase of **amplicon** generation followed by a linear phase of **amplicon** generation that utilizes only the second primer. The sample contains nucleic acid from a single cell. The T_m of the first primer is 10-20/degrees Centigrade greater than the T_m of the second primer. The concentration of the second primer is 20-100 times greater than the concentration of the first primer. The method alternatively comprises contacting the at least one nucleic acid target sequence with a first and a second oligonucleotide primer hybridizable to it; amplifying the at least one target sequence by a **polymerase chain reaction** utilizing the first and second oligonucleotide primers; and detecting **amplicon** generated from the second primer in **real time** during the PCR by means of a first hybridization probe targeted to it. The at least one nucleic acid sequence comprises at least two different nucleic acid sequences, and where the method comprises contacting each nucleic acid sequence with a first and a second nucleic acid primer hybridizable to it. The detection is performed between the PCR steps of primer extension and strand melting. The detection is performed at a temperature below the primer extension temperature. The first hybridization probe is a **molecular beacon** probe.

USE - The method is useful for amplifying stretches of DNA, including cDNA reverse transcribed from RNA, for assays, for diagnostics and other purposes. (125 pages)

L9 ANSWER 2 OF 5. CAPLUS COPYRIGHT 2003 ACS on STN

ACCESSION NUMBER: 2003:52723 CAPLUS

DOCUMENT NUMBER: 138:281776

TITLE: **Real-time PCR** with

molecular beacons provides a highly accurate assay for detection of Tay-Sachs alleles in single cells

AUTHOR(S): Rice, John E.; Sanchez, J. Aquiles; Pierce, Kenneth E.; Wangh, Lawrence J.

CORPORATE SOURCE: Department of Biology, Brandeis University, Waltham, MA, 02454-9110, USA

SOURCE: Prenatal Diagnosis (2002), 22(12), 1130-1134

CODEN: PRDIDM; ISSN: 0197-3851

PUBLISHER: John Wiley & Sons Ltd.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The results presented here provide the first single-cell genetic assay for Tay-Sachs disease based on **real-time PCR**.

Individual lymphoblasts were lysed with an optimized lysis buffer and assayed using one pair of primers that amplifies both the wild type and 1278 + TATC Tay-Sachs alleles. The resulting amplicons were detected in **real time** with two mol. beacons each with a different colored fluorochrome. The kinetics of **amplicon** accumulation generate objective criteria by which to evaluate the validity of each reaction. The assay had an overall utility of 95%, based on the detection of at least one signal in 235 of the 248 attempted tests and an efficiency of 97%, as 7 of the 235 samples were excluded from further anal. for objective quant. reasons. The accuracy of the assay was 99.1%, because 228 of 230 samples gave signals consistent with the genotype of the cells. Only two of the 135 heterozygous samples were allele drop-outs, a rate far lower than previously reported for single-cell Tay-Sachs assays using conventional methods of PCR.

REFERENCE COUNT: 14 THERE ARE 14 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 3 OF 5 BIOTECHDS COPYRIGHT 2003 THOMSON DERWENT/ISI on STN

ACCESSION NUMBER: 2002-09514 BIOTECHDS

TITLE: Detecting and quantifying minority viral mutants, especially of human immune deficiency virus resistant to protease inhibitors, by **real-time** amplification;

HIV virus and hepatitis C virus diagnosis using
polymerase chain reaction, DNA
primer and DNA probe

AUTHOR: HANCE A; CLAVEL F; LECOSSIER D; LEMIALE V
PATENT ASSIGNEE: INSERM INST NAT SANTE and RECH MEDICALE
PATENT INFO: WO 2001094644 13 Dec 2001
APPLICATION INFO: WO 2000-FR1803 9 Jun 2000
PRIORITY INFO: FR 2000-7441 9 Jun 2000
DOCUMENT TYPE: Patent
LANGUAGE: French
OTHER SOURCE: WPI: 2002-164318 [21]

AN 2002-09514 BIOTECHDS

AB DERWENT ABSTRACT:

NOVELTY - Detection and/or quantification of minority variants, having at least one **mutation**, in a heterogeneous population of viruses, present in a biological sample.

DETAILED DESCRIPTION - Detection and/or quantification of minority variants, having at least one **mutation**, in a heterogeneous population of viruses, present in a biological sample. Nucleic acids (I) are extracted from the sample and amplified by **polymerase chain reaction (PCR)**, using primers that flank a viral sequence (Ia) suspected of carrying a **mutation**. Separately a standard **amplicon** is prepared similarly, from a sequence known to carry the **mutation**. Both amplicons are then subjected to **real-time PCR** using: (i) a pair of highly conserved primers that do not differentiate between mutated and non-mutated sequences, then quantifying the number of viral (I), mutated or not, present in the sample; and (ii) a pair of primers that are **mutation** specific, and quantifying the number of **mutant** sequences in the sample. Comparison of the results of (i) and (ii) gives the proportion of **mutant** viruses in the population. INDEPENDENT CLAIMS are also included for the following: (1) pairs of primers (a) and (b); (c) and (d); (d) and (e), and (d) and (f) (a) CTTTAGCTTCCCTCAGATCACTC; (b) CCTGGCTTTAATTTTACTGGTACA; (c) GGTACAGTATTAGTAGGACCTACA; (d) TGGTACAGTTTCAATAGGACTAAT; (e) TATTAGTAGGACCTACACCAGC; and (f) AACATAATTGGAAGAAATCAGA; (2) the probe (g) CTCAGATTGGTTGCACCTTAAATTTTCC; and (3) kit for the process comprising primer pairs for the three amplifications; a probe that has conjugated to its 5' and 3'-ends, respectively, a fluorescent reporter and a fluorescence quencher, specific for the amplicons; standard (mutated) nucleic acid; products and reagents for performing **PCR** amplifications.

BIOTECHNOLOGY - Preferred Process: The minority **variant** may be any sort of virus but is particularly an RNA virus and then the first amplification is by reverse transcription **PCR**. The primers that flank the suspect viral sequences are designed to amplify mutated and non-mutated sequences with the same efficiency. The standard sequence may come from a **mutant** or engineered virus, or is any sequence that can produce an **amplicon** with the same characteristics as the **mutant** sequence. Quantification is by reaction with a probe that contains, at its 5'- and 3'-ends respectively, a fluorescent reporter and a fluorescent quencher. Preferably fluorescence is measured continuously and the number of amplification cycles required for fluorescence to pass a predetermined threshold is determined, and the numbers of total sequences and of **mutant** sequences are determined by comparing Cs with a standard curve, prepared using dilutions of standard amplicons under the same conditions.

Real-time PCR is done in presence of 3-5 mM

magnesium chloride and over 100 (preferably 200) mM of each

deoxynucleotide triphosphate, at a temperature equal to temperature for the primers used. Optionally an additional standard, similar to the first standard but without the **mutation**, is also subjected to **real-time PCR**; it allows the detection limit to be determined. Preferred **Mutation**: These introduce V82A or

L90M into the sequence of HIV protease. Preferred Primers: The sense primer that is specific for a **mutant** sequence contains at least one or two additional mismatches, apart from the **mutation**, especially a moderately destabilizing mismatch at position -2 from the 3'-end. (a) and (b) amplify the sequence containing the mutations; (c) and (d) do not discriminate between **mutant** and non-**mutant** sequences; (d) and (e) amplify the V82A **mutation** and (d) and (f) amplify the L90M **mutation**.

USE - The method is especially used to detect and quantify mutants of human immune deficiency virus that impart resistance to anti-retroviral agents that target proteases, but may also be designed for analysis of hepatitis C virus.

ADVANTAGE - The method can detect mutants at less than 1% of the total virus population.

EXAMPLE - RNA isolated from the serum of a human immune deficiency virus (HIV) patient was subjected to reverse transcription **polymerase chain reaction (PCR)** using primers that amplify the protease-encoding sequence. The **amplicon**, and an **amplicon** prepared similarly from the sequence encoding the V82A protease **mutant**, were then amplified using a common primer, either of two second primers, one specific for wild-type and the other for the V82A **mutant**, and a **TaqMan probe**. The number of amplification cycles needed for fluorescence to reach a threshold level was determined and the number of sequences initially present determined by extrapolation on a standard curve, and the results (for the two second primers) compared to calculate the percentage of **mutant** sequences. The specification lists the sequences for all primers and the probe. (49 pages)

L9 ANSWER 4 OF 5 MEDLINE on STN DUPLICATE 1
ACCESSION NUMBER: 1998250244 MEDLINE
DOCUMENT NUMBER: 98250244 PubMed ID: 9590362
TITLE: A homogeneous fluorescence assay for PCR
amplicons: its application to **real-time**
, single-tube genotyping.
AUTHOR: Whitcombe D; Brownie J; Gillard H L; McKechnie D; Theaker
J; Newton C R; Little S
CORPORATE SOURCE: Zeneca Diagnostics, Gadbrook Park, Northwich, Cheshire,
UK.. david.whitcombe@ukbla71.zeneca.com
SOURCE: CLINICAL CHEMISTRY, (1998 May) 44 (5) 918-23.
Journal code: 9421549. ISSN: 0009-9147.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199805
ENTRY DATE: Entered STN: 19980609
Last Updated on STN: 19980609
Entered Medline: 19980522
AB We have developed a method whereby a single **TaqMan probe**
can be used for many PCR reactions. We demonstrate its
application as an integrated system for the direct measurement of
allele-specific **amplicon** generation coupled to the suppression
of primer-dimer accumulation in PCR. The system uses a
5'-exonuclease assay of **amplicon** annealed fluorogenic probes
that operates in conjunction with the Amplification Refractory
Mutation System, whereby relative changes in reporter fluorescent
emission are monitored in **real-time** using an
analytical thermal cycler. We have called this system **Three-STAR**, and it
is universal in that it can either use a single probe for the detection of
any one target DNA sequence or a single pair of probes for genotyping any
bi-allelic polymorphism. **Three-STAR** is, therefore, particularly useful
for the single-tube genotype analysis of a variety of human DNA
polymorphisms and mutations.

L9 ANSWER 5 OF 5 MEDLINE on STN DUPLICATE 2

ACCESSION NUMBER: 1998324861 MEDLINE

DOCUMENT NUMBER: 98324861 PubMed ID: 9657870

TITLE: Detection of the hereditary hemochromatosis gene **mutation by real-time fluorescence polymerase chain reaction** and peptide nucleic acid clamping.

AUTHOR: Kyger E M; Krevolin M D; Powell M J

CORPORATE SOURCE: Roche Diagnostics Boehringer-Mannheim Corporation, 4300 Hacienda Drive, Pleasanton, California, 94588-2722, USA..
erich_kyger@mgc.boehringer-mannheim.com

SOURCE: ANALYTICAL BIOCHEMISTRY, (1998 Jul 1) 260 (2) 142-8.
Journal code: 0370535. ISSN: 0003-2697.

PUB. COUNTRY: United States

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 199808

ENTRY DATE: Entered STN: 19980903
Last Updated on STN: 19980903
Entered Medline: 19980825

AB Hereditary hemochromatosis (HH), an iron overload disease, is the most common known inheritable disease. The most prevalent form of HH is believed to be the result of a single base-pair **mutation**. We describe a rapid homogeneous **mutation** analysis method that does not require post-**polymerase chain reaction** (PCR) manipulations. This method is a marriage of three emerging technologies: rapid cycling PCR thermal cyclers, peptide nucleic acid (PNA) **probes**, and a new double-stranded DNA-selective fluorescent dye, Sybr Green I. The LightCycler is a rapid thermal cycler that fluorometrically monitors **real-time** formation of **amplicon** with Sybr Green I. PNAs are DNA mimics that are more sensitive to mismatches than DNA probes, and will not serve as primers for DNA polymerases. **PNA probes** were designed to compete with PCR primers hybridizing to the HH **mutation** site. Fully complemented **PNA probes** at an 18:1 ratio over DNA primers with a mismatch result in suppression of **amplicon** formation. Conversely, **PNA probes** with a mismatch will not impair the binding of a complementary primer, culminating in **amplicon** formation. A LightCycler-based rapid genetic assay has been developed to distinguish HH patients from HH carriers and normal individuals using PNA clamping technology.
Copyright 1998 Academic Press.

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FILE CONTAINS CURRENT INFORMATION.
LAST RELOADED: Sep 12, 2003 (20030912/UP).

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Accumulation of somatic **mutation** in
mitochondrial DNA extracted from
peripheral blood cells in diabetic patients.

AUTHOR: Nomiyama T; Tanaka Y; Hattori N; Nishimaki K; Nagasaka K;
Kawamori R; Ohta S

CORPORATE SOURCE: Department of Medicine, Metabolism and Endocrinology,
School of Medicine, Juntendo University, Tokyo, Japan.

SOURCE: DIABETOLOGIA, (2002 Nov) 45 (11) 1577-83.
Journal code: 0006777. ISSN: 0012-186X.

PUB. COUNTRY: Germany: Germany, Federal Republic of

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 200306

ENTRY DATE: Entered STN: 20021119
Last Updated on STN: 20030617
Entered Medline: 20030616

AB AIMS/HYPOTHESIS: A point **mutation** of **mitochondrial
DNA** at nucleotide number 3243 A to G is responsible for both the
major genetic aetiologies of the MELAS (mitochondrial myopathy,
encephalopathy, lactic acidosis and stroke-like episodes) and
mitochondrial diabetes. Otherwise, this **mutation** is also
reported to occur as an acquired somatic **mutation**, possibly due
to oxidative stress. Since diabetes can cause severe oxidative stress, we
hypothesize that the accumulation of the somatic 3243 A to G
mutation in **mitochondrial DNA** can be
accelerated by diabetes. METHODS: DNA was extracted from blood samples of
290 non-diabetic healthy subjects (age 20-60) including 98 newborn infants
and from 383 patients with Type II (non-insulin-dependent) diabetes
mellitus (age 18-80). The extent of somatic 3243 A to G **mutation**
to total **mitochondrial DNA** was detected by
real-time PCR using the **TaqMan**
Probe. RESULTS: Whereas the level of the 3243 A to G
mutation was negligible in the newborn group, it was increased in
healthy subjects who were 20 to 29 and 41 to 60 years of age, suggesting
that this **mutation** was somatic. In the diabetic patients the
mutation rate increased along with age and the duration of
diabetes. In the middle-aged group (age 41-60), the 3243 A to G
mutation accumulates fourfold higher in the diabetic patients than
the healthy subjects. Moreover, multiple regression analysis showed that
the most critical factor associated with this **mutation** in
diabetic patients was the duration of diabetes.
CONCLUSION/INTERPRETATION: Diabetes accelerates the accumulation of the
somatic 3243 A to G **mutation** in **mitochondrial
DNA**, which can accelerate the ageing process. This somatic
mutation could possibly be a new marker for estimating the
duration of diabetes.

L11 ANSWER 2 OF 3 MEDLINE on STN DUPLICATE 2

ACCESSION NUMBER: 2001234556 MEDLINE

DOCUMENT NUMBER: 21113179 PubMed ID: 11160915

TITLE: Simultaneous A8344G heteroplasmy and **mitochondrial
DNA** copy number quantification in myoclonus
epilepsy and ragged-red fibers (MERRF) syndrome by a
multiplex **molecular beacon** based
real-time fluorescence **PCR**.

AUTHOR: Suzhai K; Ouweland J; Dirks R; Lemaitre M; Truffert J;
Janssen G; Tanke H; Holme E; Maassen J; Raap A

CORPORATE SOURCE: Department of Molecular Cell Biology, Leiden University
Medical Center, Leiden, The Netherlands.

SOURCE: NUCLEIC ACIDS RESEARCH, (2001 Feb 1) 29 (3) E13.
Journal code: 0411011. ISSN: 1362-4962.

PUB. COUNTRY: England: United Kingdom

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

Single strand conformation polymorphism analysis for the
detection of point mutations in the mitochondrial DNA;
analysis of the displacement loop, tRNAIle gene and
cytochrome-b gene using the polymerase chain reaction

AUTHOR: Kim Y L; Brown M D; *Wallace D C

CORPORATE SOURCE: Univ.Emory

LOCATION: Department of Genetics and Molecular Medicine, Emory
University School of Medicine, 1462 Clifton Road, Room 446,
Atlanta, Georgia 30322, USA.

SOURCE: Anal.Biochem.; (1995) 224, 2 608-11

CODEN: ANBCA2

ISSN: 0003-2697

DOCUMENT TYPE: Journal

LANGUAGE: English

AN 1995-05193 BIOTECHDS

AB The effectiveness of single strand conformation polymorphism (SSCP) to detect all variant bases in a mitochondria DNA (mtDNA) sequence was assessed. SSCP patterns from multiple individuals, each with a different point **mutation** within the same polymerase chain reaction (PCR) fragment were examined. SSCP detected 73% of the mtDNA base substitutions distributed over 3 PCR fragments and could discriminate between point mutations in adjacent nucleotides. 3 Representative regions of the mtDNA chromosome were chosen for SSCP analysis (the displacement loop (D-loop), a hypervariable noncoding region (tRNAIle gene), and the cytochrome-b (cytb) gene). For each region, a **short PCR** fragment (240, 171, and 199 np, respectively) was made from a number of different mtDNAs, each harboring a different homoplasmic point **mutation**. Following electrophoresis on a 6% polyacrylamide gel, autoradiography was carried out. 60% (tRNAIle gene) to 75-80% (cytb gene and D-loop, respectively) of the base changes relative to an unmutated fragment were detected. Thus mtDNA SSCP analysis may be effective in screening for mtDNA point mutations. (10 ref)

Accurate, high-throughput "snapshot" detection of hMLH1 mutations by two-dimensional DNA electrophoresis.

AUTHOR: Smith W M; Van Orsouw N J; Fox E A; Kolodner R D; Vijg J; Eng C

CORPORATE SOURCE: Charles A. Dana Human Cancer Genetics Unit, Dana-Farber Cancer Institute, Boston, MA 02115-6084, USA.

CONTRACT NUMBER: 1P30AG13314-02 (NIA)

SOURCE: GENETIC TESTING, (1998) 2 (1) 43-53.
Journal code: 9802546. ISSN: 1090-6576.

PUB. COUNTRY: United States

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 199910

ENTRY DATE: Entered STN: 19991026
Last Updated on STN: 19991026
Entered Medline: 19991012

AB The human genome and related projects have resulted in the isolation of a rapidly growing number of genes that cause susceptibility to human cancer. With rare exception, these genes are large and have disease-associated mutations scattered along the length of the genes. Therefore, the development of accurate and cost-efficient **mutation** detection tests that can scan entire genes singly or in combination is warranted. hMLH1, encoding a mismatch repair enzyme, is a susceptibility gene for hereditary nonpolyposis colon cancer syndrome. This gene comprises 19 exons; mutations are scattered, typical of many susceptibility genes. Here, we present a strategy that combines extensive PCR multiplexing and two-dimensional DNA electrophoresis (Two-Dimensional Gene Scanning, TDGS) to scan accurately for mutations that lie within the exons and splice junctions of hMLH1. All target fragments, designed to have optimal melting characteristics, were prepared in a two-stage PCR--a four-plex long-distance PCR followed by **short PCR** in two multiplex groups of 10 and 11 amplicons. The mixture of amplicons was subjected to two-dimensional electrophoresis: separation by size in the first dimension and by melting characteristics in the second. Using this design, 41 samples containing known hMLH1 sequence variants or no alterations were blindly subjected to TDGS. All mutations were detected; there were no genuine false-positive or false-negative results. These results confirm that TDGS is a generally applicable, rapid, accurate, and reproducible **mutation** detection technology that would serve large-scale molecular epidemiologic studies as well as clinical molecular diagnostic purposes.

L6 ANSWER 8 OF 20 MEDLINE on STN DUPLICATE 6

ACCESSION NUMBER: 1998414506 MEDLINE

DOCUMENT NUMBER: 98414506 PubMed ID: 9740668

TITLE: Mutational scanning of mitochondrial DNA by two-dimensional electrophoresis.

AUTHOR: van Orsouw N J; Zhang X; Wei J Y; Johns D R; Vijg J

CORPORATE SOURCE: Department of Medicine, Beth Israel Deaconess Medical Center and Harvard Medical School, Boston, MA 02115, USA.

CONTRACT NUMBER: AG08812 (NIA)

AG10829 (NIA)

AG13314 (NIA)

+

SOURCE: GENOMICS, (1998 Aug 15) 52 (1) 27-36.
Journal code: 8800135. ISSN: 0888-7543.

PUB. COUNTRY: United States

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 199905

ENTRY DATE: Entered STN: 19990607
Last Updated on STN: 20000303

Entered Medline: 19990526

AB An expedient, accurate, and cost-efficient test was developed to scan critical regions of the mitochondrial genome for all possible mutations by two-dimensional DNA electrophoresis. The test involves a two-step multiplex PCR amplification: a long-distance PCR to amplify almost the entire mitochondrial genome, which then serves as template for the amplification of 25 **short PCR** fragments in two multiplex groups corresponding to regions implicated in human diseases. The mixture of fragments was subsequently subjected to two-dimensional electrophoretic separation, first by size in a nondenaturant polyacrylamide gel and then on the basis of basepair sequence in a denaturing gradient polyacrylamide gel. This latter process of denaturing gradient gel electrophoresis is a most accurate form of **mutation** detection on the basis of differences in melting behavior of **mutant** and wildtype fragments. Evaluation of the method using samples with known homoplasmic and heteroplasmic mutations, as well as CEPH pedigrees to study segregation of polymorphic variants, indicated a very high accuracy; none of the previously identified mutations and polymorphisms escaped detection, and no erroneous segregation patterns of polymorphic variants were observed. In addition, two variants were found to be novel mutations when analyzed by sequence analysis. One of these novel mutations was a heteroplasmic **mutation** in the COXIII gene that was found to segregate to homoplasmy in the next generation. Heteroplasmic mutations as low as 1% of mtDNA could still be detected. Copyright 1998 Academic Press.

1999:641022 CAPLUS

DN 131:283611

TI Catalytic nucleic acid-based diagnostic methods for **mutation** detection

IN Todd, Alison V.; Fuery, Caroline J.; Cairns, Murray J.

PA Johnson & Johnson Research Pty. Ltd., Australia

SO PCT Int. Appl., 57 pp.

CODEN: PIXXD2

DT Patent

LA English

IC ICM C12Q001-68

CC 9-2 (Biochemical Methods)

Section cross-reference(s): 3, 7

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9950452	A1	19991007	WO 1999-IB848	19990316
	W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	CA 2312288	AA	19991007	CA 1999-2312288	19990316
	AU 9935303	A1	19991018	AU 1999-35303	19990316
	AU 763135	B2	20030717		
	EP 1025266	A1	20000809	EP 1999-917023	19990316
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
	US 6361941	B1	20020326	US 1999-270140	19990316
	ZA 9902374	A	20001011	ZA 1999-2374	19990326
	CN 1327070	A	20011219	CN 2000-122574	20000603
PRAI	US 1998-79651P	P	19980327		
	WO 1999-IB848	W	19990316		
AB	This invention provides methods and kits useful for detg. whether a subject is afflicted with a disorder characterized by the presence of one or more known nucleic acid mutations. The instant methods comprise steps of nucleic acid mol. isolation, amplification, contact with one or more catalytic nucleic acid mols. specifically cleaving a target sequence present either in the case of disorder or wild-type, but not both, and detg. cleavage of the amplified segment(s). The diagnostic methods are advantageous because catalytic nucleic acids can require as few as two base pairs of specific sequence to create a cleavage site and dinucleotide cleavage sites occur naturally at a greater frequency than do restriction enzyme cleavage sites. Furthermore, mismatched primers can be used to induce cleavage sites for catalytic nucleic acids in the same way that mismatched primers have been used to induce artificial restriction enzyme cleavage sites. The method is exemplified by K-ras anal. using ribozymes designed to cleave mutant but not wild-type K-ras or using DNAzymes supplied both in trans and in cis orientation with chimeric primers.				
ST	mutation detection disease diagnosis ribozyme DNAzyme				
IT	Nucleic acid amplification (method) (DNA, primer contg. DNAzyme zymogene in cis orientation; catalytic nucleic acid-based diagnostic methods for mutation detection)				
IT	Gene, animal RL: ANT (Analyte); ANST (Analytical study) (N-ras; catalytic nucleic acid-based diagnostic methods for mutation detection)				
IT	Gene, animal RL: ANT (Analyte); ANST (Analytical study)				

(c-Ha-ras; catalytic nucleic acid-based diagnostic methods for **mutation** detection)

IT Gene, animal
 RL: ANT (Analyte); ANST (Analytical study)
 (c-Ki-ras; catalytic nucleic acid-based diagnostic methods for **mutation** detection)

IT Diagnosis
 (cancer; catalytic nucleic acid-based diagnostic methods for **mutation** detection)

IT AIDS (disease)
 Cystic fibrosis
 (catalytic nucleic acid-based diagnostic methods for **mutation** detection)

IT Ribozymes
 RL: ARG (Analytical reagent use); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
 (catalytic nucleic acid-based diagnostic methods for **mutation** detection)

IT Primers (nucleic acid)
 RL: ARG (Analytical reagent use); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
 (contg. **DNAzyme** gene for cis cleavage; catalytic nucleic acid-based diagnostic methods for **mutation** detection)

IT Ribozymes
 RL: ARG (Analytical reagent use); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
 (deoxy, 10-23; catalytic nucleic acid-based diagnostic methods for **mutation** detection)

IT Test kits
 (diagnostic; catalytic nucleic acid-based diagnostic methods for **mutation** detection)

IT Diagnosis
 (genetic; catalytic nucleic acid-based diagnostic methods for **mutation** detection)

IT **Mutation**
 (point; catalytic nucleic acid-based diagnostic methods for **mutation** detection)

IT PCR (polymerase chain reaction)
 (primer contg. **DNAzyme** zymogene in cis orientation; catalytic nucleic acid-based diagnostic methods for **mutation** detection)

IT Human immunodeficiency virus 1
 (ribozymes and DNAzymes specific for nucleic acid encoding AZT resistance; catalytic nucleic acid-based diagnostic methods for **mutation** detection)

IT 246225-74-1
 RL: ARG (Analytical reagent use); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
 (**DNAzyme** Dz1 specific for K-ras gene; catalytic nucleic acid-based diagnostic methods for **mutation** detection)

IT 246225-82-1
 RL: ARG (Analytical reagent use); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
 (**DNAzyme** Dz3 specific for K-ras gene; catalytic nucleic acid-based diagnostic methods for **mutation** detection)

IT 246225-87-6
 RL: ARG (Analytical reagent use); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
 (**DNAzyme amplicon** with cis hybridization specific for K-ras gene; catalytic nucleic acid-based diagnostic methods for **mutation** detection)

IT 246225-40-1 246225-41-2
 RL: ARG (Analytical reagent use); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
 (**DNAzyme** specific for HIV1 AZT resistance codon 215)

mutant; catalytic nucleic acid-based diagnostic methods for mutation detection)

IT 246225-36-5
 RL: ARG (Analytical reagent use); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
 (DNAzyme specific for HIV1 AZT resistance codon 41 mutant; catalytic nucleic acid-based diagnostic methods for mutation detection)

IT 246225-37-6
 RL: ARG (Analytical reagent use); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
 (DNAzyme specific for HIV1 AZT resistance codon 70 mutant; catalytic nucleic acid-based diagnostic methods for mutation detection)

IT 246225-42-3
 RL: ARG (Analytical reagent use); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
 (DNAzyme specific for HIV1 AZT resistance codon 74 mutant; catalytic nucleic acid-based diagnostic methods for mutation detection)

IT 246225-21-8 246225-26-3
 RL: ARG (Analytical reagent use); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
 (DNAzyme specific for K-ras codon 12 mutant; catalytic nucleic acid-based diagnostic methods for mutation detection)

IT 246225-27-4
 RL: ARG (Analytical reagent use); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
 (DNAzyme specific for K-ras codon 13 mutant; catalytic nucleic acid-based diagnostic methods for mutation detection)

IT 246225-29-6 246225-30-9 246225-31-0 246225-32-1 246225-34-3
 RL: ARG (Analytical reagent use); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
 (DNAzyme specific for N-ras codon 61 mutant; catalytic nucleic acid-based diagnostic methods for mutation detection)

IT 246225-53-6 246225-54-7
 RL: ARG (Analytical reagent use); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
 (DNAzyme specific for cystic fibrosis codon 508 mutant; catalytic nucleic acid-based diagnostic methods for mutation detection)

IT 246225-43-4 246225-44-5
 RL: ARG (Analytical reagent use); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
 (DNAzyme specific for cystic fibrosis codon 542 mutant; catalytic nucleic acid-based diagnostic methods for mutation detection)

IT 246225-49-0 246225-52-5
 RL: ARG (Analytical reagent use); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
 (DNAzyme specific for cystic fibrosis codon 551 mutant; catalytic nucleic acid-based diagnostic methods for mutation detection)

IT 246225-55-8
 RL: ARG (Analytical reagent use); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
 (DNAzyme specific for .alpha.1-antitrypsin codon 342 mutant; catalytic nucleic acid-based diagnostic methods for mutation detection)

IT 246225-86-5
 RL: ARG (Analytical reagent use); THU (Therapeutic use); ANST (Analytical

study); BIOL (Biological study); USES (Uses)
(DNAzyme zymogene primer 3K42Dz2 specific for K-ras gene;
catalytic nucleic acid-based diagnostic methods for **mutation**
detection)

IT 214689-42-6
RL: ARG (Analytical reagent use); THU (Therapeutic use); ANST (Analytical
study); BIOL (Biological study); USES (Uses)
(primer 3K2 specific for K-ras gene; catalytic nucleic acid-based
diagnostic methods for **mutation** detection)

IT 246225-73-0
RL: ARG (Analytical reagent use); THU (Therapeutic use); ANST (Analytical
study); BIOL (Biological study); USES (Uses)
(primer 5K42r specific for K-ras gene; catalytic nucleic acid-based
diagnostic methods for **mutation** detection)

IT 246225-79-6
RL: ARG (Analytical reagent use); THU (Therapeutic use); ANST (Analytical
study); BIOL (Biological study); USES (Uses)
(primer 5K44r specific for K-ras gene; catalytic nucleic acid-based
diagnostic methods for **mutation** detection)

IT 246225-71-8
RL: ARG (Analytical reagent use); THU (Therapeutic use); ANST (Analytical
study); BIOL (Biological study); USES (Uses)
(ribozyme I specific for K-ras gene wild-type codon 12; catalytic
nucleic acid-based diagnostic methods for **mutation** detection)

IT 246225-72-9
RL: ARG (Analytical reagent use); THU (Therapeutic use); ANST (Analytical
study); BIOL (Biological study); USES (Uses)
(ribozyme II specific for K-ras gene **mutant** codon 12;
catalytic nucleic acid-based diagnostic methods for **mutation**
detection)

IT 246225-60-5
RL: ARG (Analytical reagent use); THU (Therapeutic use); ANST (Analytical
study); BIOL (Biological study); USES (Uses)
(ribozyme specific for HIV1 AZT resistance codon 215 **mutant**;
catalytic nucleic acid-based diagnostic methods for **mutation**
detection)

IT 246225-58-1
RL: ARG (Analytical reagent use); THU (Therapeutic use); ANST (Analytical
study); BIOL (Biological study); USES (Uses)
(ribozyme specific for HIV1 AZT resistance codon 41 **mutant**;
catalytic nucleic acid-based diagnostic methods for **mutation**
detection)

IT 246225-59-2
RL: ARG (Analytical reagent use); THU (Therapeutic use); ANST (Analytical
study); BIOL (Biological study); USES (Uses)
(ribozyme specific for HIV1 AZT resistance codon 70 **mutant**;
catalytic nucleic acid-based diagnostic methods for **mutation**
detection)

IT 246225-61-6
RL: ARG (Analytical reagent use); THU (Therapeutic use); ANST (Analytical
study); BIOL (Biological study); USES (Uses)
(ribozyme specific for HIV1 AZT resistance codon 74 **mutant**;
catalytic nucleic acid-based diagnostic methods for **mutation**
detection)

IT 246225-56-9 246225-57-0
RL: ARG (Analytical reagent use); THU (Therapeutic use); ANST (Analytical
study); BIOL (Biological study); USES (Uses)
(ribozyme specific for K-ras codon 12 **mutant**; catalytic
nucleic acid-based diagnostic methods for **mutation** detection)

IT 246225-68-3
RL: ARG (Analytical reagent use); THU (Therapeutic use); ANST (Analytical
study); BIOL (Biological study); USES (Uses)
(ribozyme specific for cystic fibrosis **mutant** codon 508;
catalytic nucleic acid-based diagnostic methods for **mutation**

detection)

IT 246225-66-1
 RL: ARG (Analytical reagent use); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
 (ribozyme specific for cystic fibrosis wild-type codon 508; catalytic nucleic acid-based diagnostic methods for **mutation** detection)

IT 246225-62-7 246225-63-8
 RL: ARG (Analytical reagent use); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
 (ribozyme specific for cystic fibrosis wild-type codon 542; catalytic nucleic acid-based diagnostic methods for **mutation** detection)

IT 246225-64-9 246225-65-0
 RL: ARG (Analytical reagent use); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
 (ribozyme specific for cystic fibrosis wild-type codon 551; catalytic nucleic acid-based diagnostic methods for **mutation** detection)

IT 246225-70-7
 RL: ARG (Analytical reagent use); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
 (ribozyme specific for .beta.-globin poly(A) signal **mutant**; catalytic nucleic acid-based diagnostic methods for **mutation** detection)

IT 30516-87-1, AZT
 RL: BSU (Biological study, unclassified); BIOL (Biological study)
 (ribozymes and DNazymes specific for nucleic acid encoding HIV-1 resistance to; catalytic nucleic acid-based diagnostic methods for **mutation** detection)

IT 9041-92-3, .alpha.1-Antitrypsin
 RL: BSU (Biological study, unclassified); BIOL (Biological study)
 (ribozymes and DNazymes specific for nucleic acid encoding; catalytic nucleic acid-based diagnostic methods for **mutation** detection)

IT 246164-74-9, PN: WO9950452 SEQID: 21 unclaimed RNA 246164-75-0, PN: WO9950452 SEQID: 22 unclaimed RNA 246164-77-2, PN: WO9950452 SEQID: 23 unclaimed RNA 246164-78-3, PN: WO9950452 SEQID: 24 unclaimed RNA 246164-89-6, PN: WO9950452 SEQID: 49 unclaimed RNA 246164-92-1, PN: WO9950452 SEQID: 50 unclaimed RNA 246164-93-2, PN: WO9950452 SEQID: 51 unclaimed RNA 246164-94-3, PN: WO9950452 SEQID: 52 unclaimed RNA 246164-95-4, PN: WO9950452 SEQID: 53 unclaimed RNA 246164-96-5, PN: WO9950452 SEQID: 55 unclaimed RNA 246164-98-7, PN: WO9950452 SEQID: 56 unclaimed RNA 246164-99-8, PN: WO9950452 SEQID: 58 unclaimed RNA 246165-00-4, PN: WO9950452 SEQID: 59 unclaimed RNA 246165-01-5, PN: WO9950452 SEQID: 60 unclaimed RNA 246165-02-6, PN: WO9950452 SEQID: 61 unclaimed RNA 246165-03-7, PN: WO9950452 SEQID: 62 unclaimed RNA 246165-04-8, PN: WO9950452 SEQID: 63 unclaimed RNA 246165-05-9, PN: WO9950452 SEQID: 64 unclaimed RNA 246165-06-0, PN: WO9950452 SEQID: 65 unclaimed RNA 246165-07-1, PN: WO9950452 SEQID: 66 unclaimed RNA 246165-08-2, PN: WO9950452 SEQID: 67 unclaimed RNA 246165-09-3, PN: WO9950452 SEQID: 68 unclaimed RNA 246165-11-7, PN: WO9950452 SEQID: 69 unclaimed RNA 246165-15-1, PN: WO9950452 SEQID: 71 unclaimed RNA 246165-17-3, PN: WO9950452 SEQID: 72 unclaimed RNA 246165-23-1, PN: WO9950452 SEQID: 73 unclaimed RNA 246165-24-2, PN: WO9950452 SEQID: 74 unclaimed RNA 246165-25-3, PN: WO9950452 SEQID: 75 unclaimed RNA 246165-26-4, PN: WO9950452 SEQID: 76 unclaimed RNA 246165-27-5, PN: WO9950452 SEQID: 77 unclaimed RNA 246165-31-1, PN: WO9950452 SEQID: 78 unclaimed RNA 246165-32-2, PN: WO9950452 SEQID: 79 unclaimed RNA 246165-33-3, PN: WO9950452 SEQID: 80 unclaimed RNA 246165-34-4, PN: WO9950452 SEQID: 81 unclaimed RNA 246165-36-6, PN: WO9950452 SEQID: 82 unclaimed RNA 246165-47-9, PN: WO9950452 SEQID: 83 unclaimed RNA 246165-50-4, PN: WO9950452 SEQID: 84 unclaimed RNA 246165-61-7, PN: WO9950452 SEQID: 86 unclaimed RNA 246165-62-8, PN: WO9950452 SEQID: 87 unclaimed RNA 246165-63-9, PN: WO9950452 SEQID: 88 unclaimed RNA 246165-64-0, PN: WO9950452 SEQID: 89 unclaimed RNA 246165-66-2, PN: WO9950452 SEQID: 90 unclaimed RNA 246165-67-3, PN: WO9950452 SEQID: 92 unclaimed RNA 246165-68-4, PN: WO9950452 SEQID: 95 unclaimed RNA

246165-69-5, PN: WO9950452 SEQID: 96 unclaimed RNA 246165-71-9, PN:
WO9950452 SEQID: 99 unclaimed RNA 246165-72-0, PN: WO9950452 SEQID: 100
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246165-75-3, PN: WO9950452 SEQID: 103 unclaimed RNA 246165-76-4, PN:
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246165-82-2, PN: WO9950452 SEQID: 115 unclaimed RNA 246165-83-3, PN:
WO9950452 SEQID: 116 unclaimed RNA 246165-84-4, PN: WO9950452 SEQID: 117
unclaimed RNA 246165-85-5, PN: WO9950452 SEQID: 118 unclaimed RNA
246165-86-6, PN: WO9950452 SEQID: 119 unclaimed RNA 246165-87-7, PN:
WO9950452 SEQID: 120 unclaimed RNA 246165-88-8, PN: WO9950452 SEQID: 121
unclaimed DNA 246165-90-2, PN: WO9950452 SEQID: 123 unclaimed DNA

RL: PRP (Properties)

(unclaimed nucleotide sequence; catalytic nucleic acid-based diagnostic
methods for **mutation** detection)

IT 246165-14-0 246165-55-9 246165-89-9

RL: PRP (Properties)

(unclaimed sequence; catalytic nucleic acid-based diagnostic methods
for **mutation** detection)

RE.CNT 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD

RE

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- (2) John Hopkins School Of Medicine; WO 9519448 A 1995 CAPLUS
- (3) Phylactou, L; Biochem Biophys Res Commun 1998, V249(3), P804 CAPLUS
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- (5) Us Secretary Of Health & Human Services; WO 9909162 A 1999 CAPLUS

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